AMENDMENTS TO THE DRAWINGS

The attached two (2) sheets of the drawings (Figure 3) include the following changes:

Figure 3 has been amended by deleting the asterisk and the pound sign, and placing the language "P<0.01" and "P<0.05" into the figure.

Attachments: Replacement Sheet for Figure 3.

REMARKS

Claims 7-11 are all the claims pending in the application.

Claim 7 has been amended to recite the elected condition and Claim 9 has accordingly been canceled. Claim 7 has also been amended to recite the specific site of administration, as supported, for example at page 9, lines 25-27 of the original specification. In addition, Claim 7 has been amended as suggested by the Examiner to clarify that the vector is administered in a therapeutically effective amount and to clarify that the vector contains the gene coding sequence.

Claim 8 has been amended to delete the option of the membrane being further fused to Sendai particles and that recitation forms the basis of new Claim 10.

New Claim 11 is supported at, for example, p.12, l.18 - p.13, l.8 of the original specification.

Accordingly, no new matter is added.

I. Formal Matters

A. Priority

The Examiner noted that the claim for benefit should be updated and the filing date of application No. 09/029,497 should be corrected.

In response, Applicants have updated the claim for benefit.

B. Information Disclosure Statements

The Examiner has signed and returned the PTO forms SB/08 submitted with the Information Disclosure Statements filed July 9, 2003, October 9, 2003, and January 13, 2005 and September 26, 2005. The Examiner indicated that while all references cited in the Information Disclosure Statement filed July 9, 2003 have been considered, several citations have been crossed out and will not appear on the face of any patent that might issue. The references were crossed out because the citation is in improper format or the reference is not a publicly available document.

Submitted herewith is a PTO form SB/08 properly citing the English language references that were crossed out. The Examiner is requested, respectfully to initial and sign the form so that the references can appear on the face of the patent.

C. Drawings

The drawings were objected to because drawings 12-15 each contain two panels, but the brief description does not indicate what information applies to which panels. Figures 2 and 3 were also objected to because the Examiner considers that the meaning of the pound sign is unclear.

In response, a replacement Figure 3 clarifying what the pound sign and asterisks stand for, as supported in the paragraph bridging pages 25-26 of the original specification, is submitted herewith, and the description of Figures 2 and 12-15 has been amended to clarify the meaning of the pound sign and asterisks as supported in the Examples.

II. Detailed Action

A. Claim Rejections - 35 U.S.C. § 112, Second Paragraph

Claim 8 was rejected as indefinite because it contains the optional limitation that the membrane of the liposome may be fused to attenuated Sendai virus particles.

This rejection has been overcome by deleting the recitation from Claim 8 and placing it in a new dependent Claim 10.

B. Claim Rejections - 35 U.S.C. § 112, First Paragraph

Claims 7-9 were rejected under 35 U.S.C. § 112, first paragraph as lacking enablement for their full scope.

The Examiner stated that the specification is enabling for a method of gene therapy for treating restenosis after percutaneous transluminal coronary angioplasty by inducing angiogenesis in the heart, comprising administering by direct coronary injection into the heart muscle of the subject a Sendai virus (HVJ) liposome encapsulated plasmid vector comprising a mammalian HGF gene coding sequence operably linked to a constitutive promoter, and wherein

cells of the heart muscle express the HGF protein, which protein then acts to increase angiogenesis in the heart muscle.

The Examiner asserted that the specification is not enabling for any cardiac disease, any vector, and any promoter or for non-local administration.

More specifically, the Examiner asserted that use of a single vector does not enable the use of any other vector, because the effectiveness of gene therapy is known to vary widely depending on the vector used. In particular, the Examiner stated that HVJ-liposomes are known to greatly increase transformation efficiency (citing Taniyama et al, (2001) Circulation, 104: 2344-50).

The Examiner also stated that HGF is only considered effective for increasing proliferation of blood vessel endothelial cells local to the site of expression (citing Miller, et al. (1995) FASEB J. 9:190-199).

With regard to the use of promoters, the Examiner indicated that a person of ordinary skill in the art would reasonably predict that the claimed method would only be therapeutically effective if constitutive promoters were used to express high levels of protein.

For the following reasons, this rejection is overcome and/or traversed.

Claim 7 has been amended to recite the elected indication, namely myocardial infarction. It is believed that the Exmainer made a clerical error by referring to treating restenosis after percutaneous transluminal coronary angioplasty.

As to the remaining issues, submitted herewith is a coy of the Declaration of Dr. Morishita, originally filed February 11, 2000 in the grandparent case.

1. Vectors

Applicants respectfully traverse the Examiner's position regarding enablement of expression vectors, for at least the following reasons.

As noted in detail at pages 14-16 of the Declaration of Dr. Morishita, the present specification indicates that any expression vector would be expected to function in the present invention.

In particular, the Examples in the present specification show that gene therapy using the HVJ-liposome method is highly effective, and that HGF is an extremely potent cell growth stimulator. Accordingly, the specification states that any dosage forms of the HGF gene, including viral expression vectors and naked DNA, would be effective for gene therapy. Further, the literature evidence cited and summarized in the Declaration confirms that HGF gene therapy using the adenoviral vector is effective, and also that the naked-DNA method is effective for gene therapy using the HGF gene. Thus, the present specification enables the use of any expression vector for HGF gene therapy.

2. Promoter

With regard to promoters, the Examiner has indicated that the specification enables gene therapy using HGF operably linked to a constitutive promoter (see above).

However, Applicants respectfully submit that although a constitutive promoter was used in the Examples of the present specification, any kind of promoter that can function to induce the expression of the HGF gene in the site wherein the HGF gene has been administered can be used in the present invention, regardless of whether the promoter is constitutive or non-constitutive. This conclusion is supported by the disclosure of the present application, in view of common knowledge among those of ordinary skill in the relevant art at the filing date of the application. Furthermore, it is apparent that, once the HGF gene has been expressed to produce HGF protein, the HGF protein can exhibit pharmacological activities such as angiogenesis.

Therefore, because the claimed invention is enabled using any kind of promoter, without limitation to a constitutive promoter, Applicants submit that Examiner's position regarding promoters is incorrect.

3. Administration site

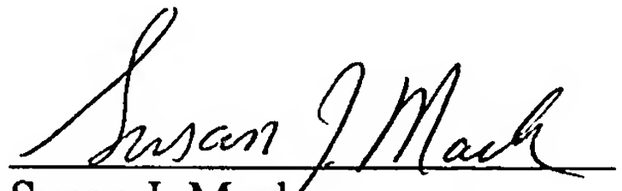
The Examiner has indicated that the specification enables local treatment at the site of administration. In this regard, Applicants have amended the claims to recite methods for treating myocardial infarction by direct intracoronary injection into the heart muscle.

However, as discussed at page 13 of the Declaration of Dr. Morishita, HGF gene therapy according to the present invention is also effective when administrated by other routes. Applicants note that the claims have been amended merely to further prosecution and for the purpose of obtaining patent protection for the subject matter recited in the present claims. Therefore, the claim amendment described above does not indicate Applicants' admission of the Examiner's assertion that the claimed invention does not satisfy the enablement requirement.

In view of the above, reconsideration and allowance of this application are now believed to be in order, and such actions are hereby solicited. If any points remain in issue which the Examiner feels may be best resolved through a personal or telephone interview, the Examiner is kindly requested to contact the undersigned at the telephone number listed below.

The USPTO is directed and authorized to charge all required fees, except for the Issue Fee and the Publication Fee, to Deposit Account No. 19-4880. Please also credit any overpayments to said Deposit Account

Respectfully submitted,



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Date: August 18, 2006

U.S. Patent Application No. 10/615,292
Inventor(s): Ryuichi MORISHITA, et al.
Filed: July 9, 2003 Art Unit: 1633
For: MEDICAMENT COMPRISING HGF GENE
Attorney Docket: Q75927
Sughrue Telephone No.: 202-293-7060
REPLACEMENT DRAWING Figs. 3-4
ANNONTATED SHEET

FIG.3

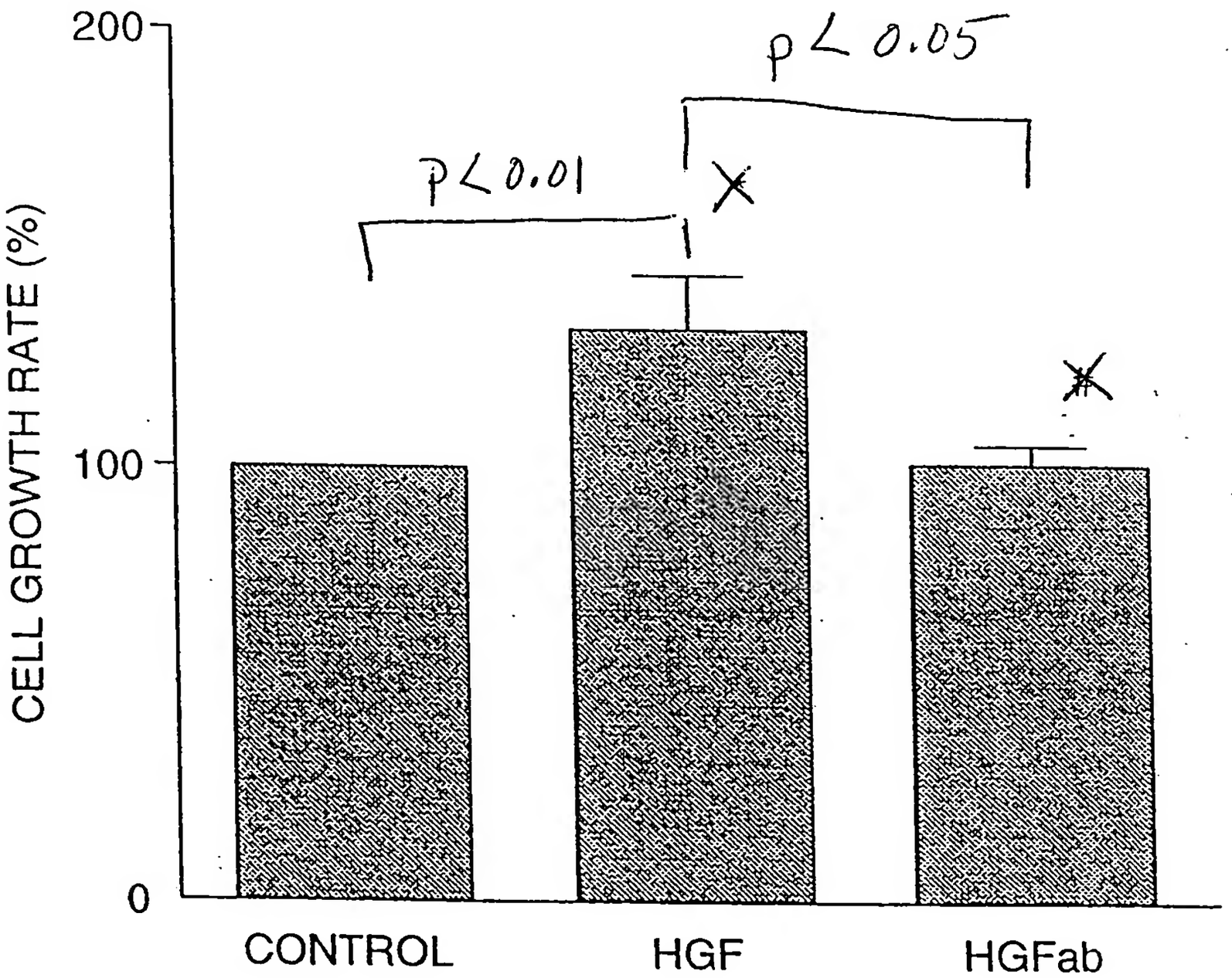

FIG.4